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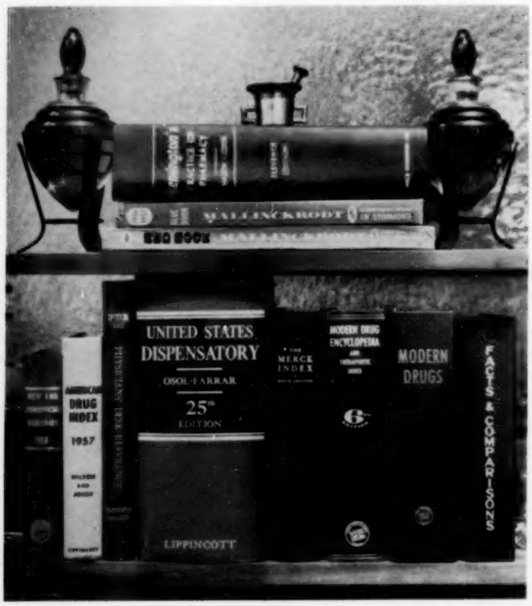

USEFUL SOURCES OF DRUG INFORMATION

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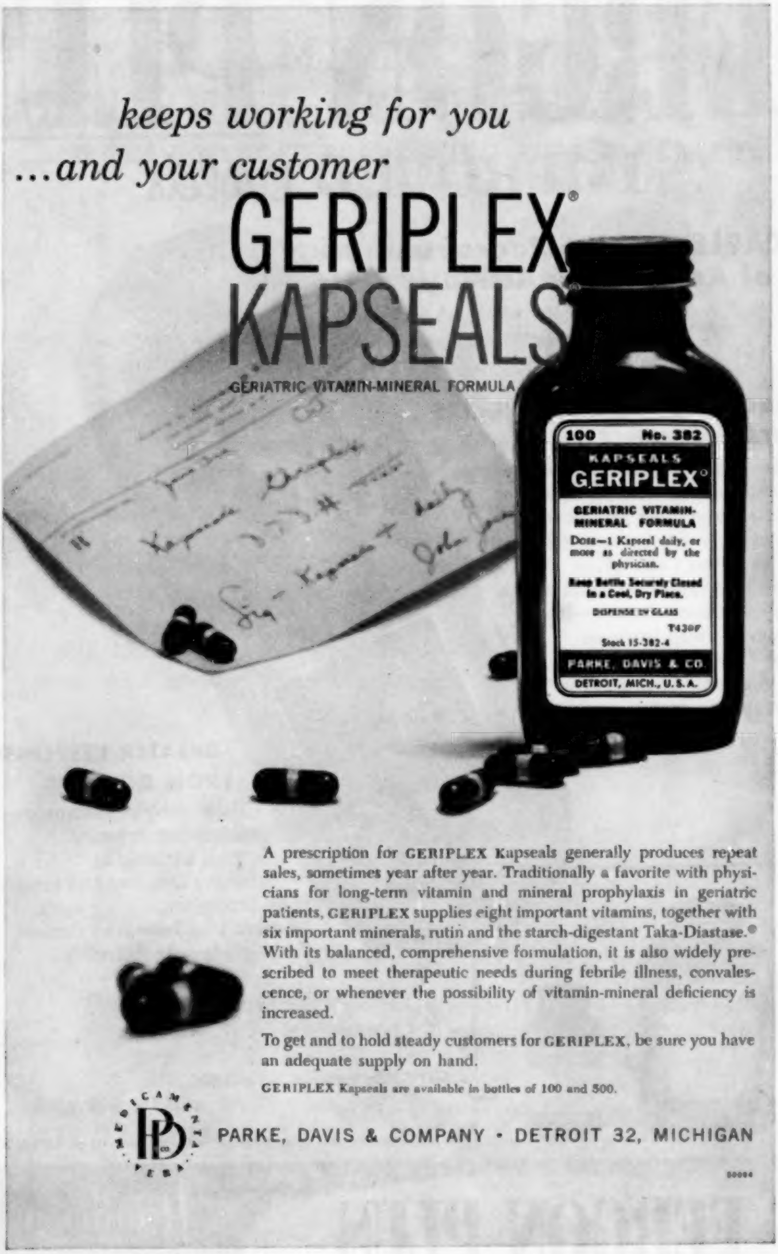

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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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E D I T O R I A L

SOURCES OF INFORMATION

IT has often been said that next in importance to knowing some fact is where to look to find it. Third in importance, quite certainly, would be the ready availability of the textbook or reference in which such information was to be found.

Every scientific and technical field, today, has a vast literature of its own, and its complexities stagger even those who have devoted a lifetime to their particular specialty. The student or the novice would be discouraged at the very outset were it not for his ignorance of the whole and the great blessing of youthful enthusiasm and energy. In spite of this both the novice and the expert need a well-stocked reference library if the questions which arise daily are to be answered with speed and accuracy.

The pharmacist and the physician, as well as those closely allied to these professions, have one of the most confusing problems of all, namely, establishing the identity, nature and uses of the many thousands of drugs. Almost every drug has at least two names—generic and proprietary, and some have as many as fifteen or twenty names. Even in our national pharmacopeias there is no uniformity of nomenclature, and generic names probably by careful intent are coined so as to be almost unpronouncable and even more difficult to remember. By reason of the astronomical number of drug names it is unavoidable that some of quite different identity have names which are identical except for a letter or two. As a current example one could cite Albamycin and Albomycin.

No other field, to our knowledge, has the confusion in nomenclature which we suffer daily in pharmacy, and there seems to be no prospect other than a worsening of the situation as new drugs are developed. For this reason the gathering together of sources of drug information assumes greater importance day by day. The collection of foreign texts and references must be a part of this, as communication with other lands is as common today as it was between New York and Washington at the turn of the century.

Recognizing the need for an authoritative and up-to-date international bibliography of texts and references on drugs, a Committee on Drug Information Sources was organized under the chairmanship of Miss Anne McCann, a member of the library staff of the Squibb Institute for Medical Research. This Committee functions as a part of the Pharmaceutical Section, Science-Technology Division of the Special Libraries Association. The Committee plans to publish a comprehensive list of Drug Information Sources broken down into country of origin. This month the first of the series covers those in the United States and Canada.

This series should prove an invaluable guide to those who wish to assemble a collection of references giving information on drugs. Librarians in our colleges of pharmacy, medicine and dentistry, those in government agencies and those in industry should be particularly interested. It is almost certain that no library now in existence has all of the books and references that will be described in this series. The complete collection would not be prohibitive in cost and we hope that some few libraries will make it one of their important projects.

The journal staff is pleased to have this medium selected for the publication of this series. We compliment the Pharmaceutical Section for its great service in creating this project and the Committee for bringing it into fruition. Our readers are certain to find each installment of interest and we commend it to their attention.

L. F. Tice

DRUG INFORMATION SOURCES *

PHARMACISTS, physicians, nurses, veterinarians, dentists, pharmaceutical industry personnel and the librarians serving all of these groups need continuous sources of information about drugs, their chemistry, their pharmacology, their clinical effects, and their market status. Excellent national lists have been published in the pharmaceutical journals of the world but at the present time no comprehensive international bibliography exists.

It is with the purpose of providing a comprehensve world listing of the various sources of information about drugs that the Pharmaceutical Section, Science-Technology Division, Special Libraries Association, has compiled its "Drug Information Sources" bibliography.

"Drug Information Sources" will be published monthly in the pages of *American Journal of Pharmacy.* This the first issue includes the source books of the United States and Canada. Subsequent issues will list sources of France, England, Scandinavian countries, Germany and every country from which information can be obtained. The bibliography will be revised, as needed, in order to keep it up to date. It is hoped that new sources of drug information will be called to the attention of the Drug Information Sources Committee so that the compilation may be made as comprehensive as possible.

Books to be included may be drug encyclopedias or price lists in which drugs are listed alphabetically by proprietary name; therapeutic guides in which drugs are mentioned as remedies; dispensatories, if they are up-to-date and include the common and proprietary names under which drugs are sold. No single source book in any country nor any single form of source book supplies all available information about drugs used and sold in that country. This bibliography will therefore list for each country those books which collectively identify the drugs used in that country and report for each drug its composition, variant names, actions, indications, dosage, manufacturer, supply and price. Compilations which are international in scope, such as *Unlisted Drugs,* will be included under the country of publication.

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* A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

Source books which report drugs by their common, generic or proprietary names, rather than their official names, will be stressed. In this respect "Drug Information Sources" will supplement the Strieby-Spencer list of pharmacopoeias (National and international pharmacopoeias; a checklist, compiled by Mrs. Irene M. Strieby and Marjory C. Spencer. *Bulletin of the Medical Library Association* 40: 153-161 (April 1952); to be supplemented in 1957).

The Pharmaceutical Section is grateful to the *American Journal of Pharmacy* for undertaking the publication of "Drug Information Sources". It is hoped that this bibliography will prove to be a useful tool in the documentation of pharmaceutical science.

UNITED STATES

The Dispensatory of the United States of America. 25th ed., edited by Arthur Osol and George E. Farrar, Jr. Philadelphia, Lippincott, 1955. 2139 pp. $25.00.

A one-volume encyclopedia containing comprehensive monographs on individual drugs and general survey articles on pharmacologic classes of drugs. Monographs include description, history, standards and tests, assay methods, actions, uses, toxicology and dosage; they are documented by literature references. Official, generic, proprietary and chemical names are given in the monographs. Monographs are arranged in three sections: drugs listed in the United States Pharmacopeia, National Formulary [U. S.] and British Pharmaceutical Codex; drugs not listed in these official compilations; drugs used in veterinary practice. Official, generic and proprietary names are listed alphabetically in the general index, but chemical names are generally not included.

Remington's Practice of Pharmacy. 11th ed., edited by Eric W. Martin and E. Fullerton Cook. Easton, Penna., Mack Pub. Co., 1956. 1707 pp. $18.00.

A comprehensive reference book covering the entire field of pharmacy and pharmaceuticals. The sections on drugs are arranged according to chemical structure. Chapters summarize history, preparation, properties and uses of groups of drugs having like structure or pharmacologic action; each summary is followed by monographs on

official drugs in the group. Monographs report identification, preparation, sources, actions and uses; description, tests and assay and storage procedures are reprinted from official souces and literature references to synthesis and assay are frequently included. Comprehensive lists of chemical names and other synonyms are included and the monographs are followed by lists of unofficial preparations and specialties, the latter with their manufacturers. Official, generic and proprietary names are listed alphabetically in the general index.

Modern Drug Encyclopedia and Therapeutic Index (Gutman). 6th ed., edited by Marion E. Howard. New York, Drug Publications, 1955. 1477 pp. $15.00 including supplements.

Monographs are listed alphabetically by proprietary name of drug or combination. They include manufacturer, chemical name and formula, generic name, description and composition, action and uses, method of administration, precautions and forms. Separate sections list biologicals and allergens. There are an index by indications, a generic name index and a directory of manufacturers with their products. The general alphabetic index is inclusive except for chemical names. The *Encyclopedia* is supplemented by monographs in *New Modern Drugs,* a bimonthly periodical published by Drug Publications.

American Medical Association. Council on Pharmacy and Chemistry. New and Nonofficial Remedies, 1956. Philadelphia, Lippincott, 1956. 540 pp. $3.35.

An annual compilation of reports on new drugs evaluated by the Council. Monographs are arranged in broad groups classified by pharmacologic effects. They are entered under the generic names of individual drugs and include for each drug its chemical or biological identity, physical properties, actions, uses, dosages and proprietary names under which it is sold. Drugs are exempt from listing after twenty years as official drugs or after action and uses are well-known; a reference to the latest monograph is retained in the index. A general alphabetic index to generic and proprietary names is included. A cumulative bibliography of unaccepted products was published annually until 1953. Supplemented by *Reports* of the Council in the Journal of the *American Medical Association.*

Unlisted Drugs. Vol. 1 (1949) to date. Editor: Miss Winifred Sewell. New Brunswick, N. J., Special Libraries Association, Science-Technology Division, Pharmaceutical Section. $8.00 per year.

This monthly cooperative publication of the Pharmaceutical Section lists new drugs found in literature or advertising when no entries are located for them in *Modern Drug Encyclopedia, New and Nonofficial Remedies* or other standard sources. Entries are made for experimental compounds under their research numbers as well as for marketed products. Entries include brief statement of composition, manufacturer, action, dosage and source of information. A cumulative alphabetic index is published for the first half of each year and for the full year.

The Merck Index of Chemicals and Drugs; An Encyclopedia for the Chemists, Pharmacist, Physician, and Allied Professions. 6th ed. Rahway, N. J., Merck & Co., 1952. 1167 pp. $8.00.

Entries on individual drugs are listed alphabetically, usually by chemical name, with cross-references from alternate chemical, generic, trivial and proprietary names. Entry includes brief description, statement of chemical properties, medical and veterinary uses. The emphasis is on basic chemistry; structural formulas and references to papers on preparation are frequently included. Drug combinations are not included.

The American Drug Index. By Charles O. Wilson and Tony Everett Jones. Philadelphia, Lippincott, 1956. 576 pp. $5.00.

Drugs are listed alphabetically by proprietary, official or generic names with cross-references from alternate names and from individual drugs to names of combinations in which they will be found. The entry includes the generic name, chemical name, manufacturer, a brief statement of composition, dosage, use, pharmaceutical forms and how supplied. Comparative tables of combinations are inserted throughout the text.

Facts and Comparisons. Edited by E. K. Kastrup. St. Louis, Mo., Facts and Comparisons Inc. 1953 to date. Looseleaf. 316 pp. and index. $12.00 with revision sheets for one year; revision sheets, $5.00 per year.

A looseleaf listing of drugs arranged in groups of products classified broadly according to use. Manufacturer, composition, recommended dosage, cost index and general usage are given for each drug. Constituents are listed in tabular form to facilitate comparison. An annual product index lists all trade and generic or official names in alphabetical order. There is also an alphabetic index to the pharmacologic groups. Information is kept up-to-date by monthly revised pages and additions to the annual index.

PDR: Physicians' Desk Reference to Pharmaceutical Specialties and Biologicals. 10th ed. Oradell, N. J., Medical Economics, Inc., 1955. Var. paging.

An annual listing of drugs arranged in several sections; the pink section is a comprehensive alphabetic listing of brand name products and a list of manufacturers with their products. The yellow section is a drug, chemical and pharmacological index to drugs and the blue section, a therapeutic index. The white section is a list of the major products of 149 manufacturers, with information on composition, action, uses, administration, dosage, contraindications and supply of each drug.

Accepted Dental Remedies. Including a list of accepted products together with other information compiled to promote rational therapeutics in dentistry. 21st ed. Chicago, American Dental Association, 1956. 206 pp. $2.00.

An annual listing of commercial products accepted by the American Dental Association Council on Dental Therapeutics. The products are arranged in sections by class of drug or broad uses. Information includes description, properties, general discussion of class of product, action, usage, and dosage. Trade names and manufacturers are given for some of the products. General literature references are cited at the end of each section. A general index and index to distributors are also included.

Veterinary Drug Encyclopedia and Therapeutic Index. 4th ed., edited by H. C. Stephensen and S. G. Mittelstaedt. New York, Drug Publications, 1956. 374 pp. $6.00.

A companion volume for veterinarians to the *Modern Drug Encyclopedia* for physicians. The information is arranged in three sections: an alphabetic listing of drugs, biologicals and foods by trade name with information about manufacturer, identity, administration, contraindications and supply; a manufacturer's directory and index; and a detailed therapeutic index. The year of addition of a new preparation is indicated.

1956-1957 Blue Book. New York, American Druggist, 1956. 690 pp. $8.00.

An annual price list of drug products, giving for each its manufacturer, sizes and wholesale and retail prices. Prescription items and narcotics are identified. The product list includes in one alphabet trade-named drugs and generic-named drugs as well as lists of products under the manufacturer's name. Price changes and new products are listed in the monthly issues of *American Druggist*.

Drug Topics Red Book. 1957 edition. New York, Topics Publishing Co., 1956. 629 pp. $9.00.

An annual price list of drug products, giving for each its manufacturer, sizes and price to consumer and retailer. The product list includes in one alphabet trade-named drugs and generic-named drugs as well as lists of products under the manufacturer's name. Price changes and a new products are listed in the bi-weekly issues of *Drug Topics*.

CANADA

New Products Index. Vol. 1 (1951) to date. Edited by F. N. Hughes and G. C. Walker. Toronto, Canadian Pharmaceutical Journal. $2.00 per volume.

This serial publication lists alphabetically proprietary-name and generic-name products distributed in Canada. For each drug manufacturer, description, indications, administration and supply are provided. Veterinary products are included with products for human use. Each volume includes cumulative product, therapeutic and manufacturer's indexes to the products listed in all volumes published to

date. Monographs from Volume 1, however, were revised and incorporated in Volume 10 (1956) so that Volume 1 may be discarded. Products discontinued by the manufacturer are dropped from the cumulative indexes.

V-I; Vademecum International 1957. Montreal, J. Morgan Jones Pubns., 1956. Var. pagings.

An annual listing of pharmaceutical specialties and biologicals in three sections: the white section reports composition, uses, dosage, supply and availability of company literature for the major products distributed in Canada. Entries are grouped under name of manufacturer and are alphabetically indexed. The yellow section is a therapeutic and pharmacologic index to products listed in the white section and the pink section is a comprehensive list of products by manufacturer. Editions are published in English and French. (It is a continuation of *Pharmaceutical Guide* and *Guide Pharmaceutique.*)

Drug Index 1957. Toronto, Maclean-Hunter Pub. Co., 1956. 56 pp. (Part 2, Oct. 15, 1956, issue of Drug Merchandising)

Alphabetic list of prescription specialties available in Canada with their manufacturers or distributors. New items and changes published in regular issues of *Drug Merchandising.*

The Committee on Drug Information Sources has the following members:

ANNE MCCANN, *Chairman,* ELIZABETH BOYKIN, HAROLD OATFIELD, JAMES L. OLSEN, JR., MAXINE PAINTER, CLARA ROBSON, WALTER SOUTHERN and IRENE STRIEBY.

A limited number of reprints are available for distribution by the Committee at 30¢ each. Requests should be sent to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J. Payment should accompany order.

Regular distribution will not be undertaken by the Section. Individuals and libraries wishing to ensure continued receipt of "Drug Information Sources" may do so by entering subscriptions to *American Journal of Pharmacy.*

Correspondence about "Drug Information Sources" should be directed to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J. (Ed.)

THE RATE OF HEATING OF CORN OIL TO STERILIZING TEMPERATURES

By Kenneth E. Avis * and Louis Gershenfeld **

IN a study reported previously (1), the authors noted that the use of certain bacteria-excluding filters cannot be relied upon for prolonged use in the sterilization of oils. A survey of 59 American manufacturers of parenteral products, included as a part of that study, revealed that heating methods were employed more frequently for the sterilization of oils than were filters. An important problem in the heat sterilization of oils is considered in this present paper, the second in a series. The problem, frequently given inadequate consideration, is that of the time required for particular volumes of oil to reach the sterilizing temperature in the chambers wherein they are placed.

A number of authors (2, 3, 4, 5) have published data substantiating the practice of sterilizing anhydrous oils and oleaginous materials by means of dry heat in a hot air oven. The combination of time and temperature recommended to accomplish sterilization has varied from not less than four hours at 140° C. to from one to two hours at 160° C. However, in none of these reports was consideration given to the time required for a given volume of oil to reach the designated temperature.

The Extra Pharmacopoeia (6) quoted an unidentified report that 100 ml. of oil required 72 minutes for the oil to reach 150° C. after the oven had reached that temperature. No details were given concerning the container or the type of oven used. Perkins reported (7) that an oleaginous material, petroleum jelly, required 165 minutes for 4 oz. of the material in a glass jar to reach 160° C., starting at room temperature. The type of oven employed and other details were not specified.

A study of the rate of heating of various volumes of oil up to 400 ml. in a gravity convection type hot air oven has been reported by Janot and Ruoss (8). They found that the volume of oil in a single

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** Professor of Bacteriology and Director of the Bacteriology Department, Philadelphia College of Pharmacy and Science.

container (glass ampul) and the surface area of oil exposed to the hot air affected the heating rate, that the thickness of the glass wall of the containers had no significant effect, and that pre-heating the oven markedly decreased the time required for the oil to reach the maximum temperature, usually about 5° C. below the temperature recorded at the outlet of the oven chamber.

Very little data have been found in the literature as to the time required to heat various volumes of oil to sterilizing temperatures, particularly of volumes greater than those mentioned above. In our study, most of the experimental data reported deal with volumes of oil between 1000 ml. and 3000 ml., although volumes as small as 10 ml. were also employed. Data have been accumulated to show some of the factors involved in the rate of heating of oils in a hot air oven and, to a limited extent, in an autoclave with free-flowing steam. However, many variables have been encountered which affect the heating rate of a given volume of oil.

Theoretical Considerations

It is well known that the transfer of heat from one object to another involves one or more of the thermal processes of conduction, convection, and radiation. In a hot air heating situation, a given container of oil receives radiant heat energy from the heating elements, the oven walls, and other containers of oil. Heat energy passes by conduction through the walls of the container. Convection plays a significant part in the transfer of heat energy through the air of the chamber and through the oil within the container. As the temperature of the oil increases and its viscosity decreases, the effect of convection heating within the oil becomes more pronounced. Heat transfer is also known to be a dynamic situation. Thus, a given container of oil loses heat energy at the same time that it gains such energy. The quantity of material being heated and its thermal characteristics, convection flow patterns within the chamber and within the oil in a container, as well as numerous other factors, have an effect upon the efficiency of heat transfer.

In the study reported in the following pages, the interplay of the processes and factors involved in heat transfer have been found to be quite complex. In most instances, it has not been possible to distinguish clearly the effect of one process or factor from another.

Apparatus

The hot air oven used for heating the oil samples was a Boekel gravity type electric sterilizing oven having internal dimensions of 15″ × 25″ × 18″. The walls were filled with 3″ of glass wool insulation. The heating coils were located at the bottom of the oven chamber along each of the four sides. A perforated metal sheet, solid in the center of the chamber, was located directly above the coils. The metal grill flooring on which the samples of oil were placed was approximately 3″ above this sheet. The thermometer was located in the outlet at the top center of the chamber. The sensitivity of the thermostatic control at the thermometer, as noted by the manufacturer, was ± 2° C. when the temperature was at 170° C. with equipment in the oven. The operating uniformity (variance throughout the working shelf space) was given by the manufacturer as ± 22° C. at 170° C. with equipment in the oven. Such wide temperature variance is common to gravity type hot air sterilizing ovens.

The autoclave used to heat the oil samples with free-flowing steam was a triple-walled, round, horizontal Barnstead model having an internal diameter of 22″ and a length of 35″. Steam was generated in a boiler separate from the autoclave.

The thermocouples used to determine the temperatures of the oil samples were of copper-constantan and were connected through a multiple switch to a Leeds and Northrup student potentiometer with a Rubicon Spotlight Galvanometer as the null point indicator. Six working thermocouples and a reference thermocouple were employed. The reference thermocouple was attached to the bulb of the thermometer in the outlet at the top of the oven chamber. A standardization graph was plotted from data correlating the voltage shown on the slide wire of the potentiometer to temperature difference between the reference and the working thermocouples. It gave a straight line.

The containers used for the oil samples included a Pyrex test tube (18 × 165 mm.), various sizes of Pyrex Griffin beakers (150, 400 and 1000 ml.), Pyrex narrow mouth Erlenmeyer flasks (125 and 500 ml.), 1 liter (100 × 130 mm.) and 2 liter (130 × 180 mm.). Pyrex heavy wall bottles, and cans of various sizes and shapes (50 to 150 mm. diameter × 60 to 230 mm. high). The cans either had a lid closure of the same metal as the body of the can or they had been opened by cutting around the perimeter of the top end of the can allowing a metal hinge to remain so that the end could be relowered

as a lid. Beakers were covered over the top with aluminum foil. Flasks and bottles were closed with vented stoppers. In all containers, the thermocouples were inserted through an open end glass tube which was, in turn, held in the center of the container by means of a vented stopper or other loose closure. In no instance was the container opening left exposed to the air.

Two modifications were made in the accessories to the oven as the experiments progressed. In order to circulate the hot air in the oven, a fan with four 2″ blades was attached to a shaft inserted through a hole in the wall of the oven into the upper, rear, left-hand corner of the oven. The shaft was then attached to a small motor outside of the oven. The second modification was provided during a few experiments in which the oil in one can was stirred. This was accomplished by passing a cord from a motor driven eccentric over a pulley and then down into the oven through the top outlet adjacent to the thermometer. The end of the cord in the oven was attached to one leg of a tripod. The other legs had been removed. The ring of the tripod was thus pulled up and down within the can of oil through a stroke of about 5″ at a rate of about 15 strokes a minute.

Method

The six working thermocouples were inserted through the outlet in the top of the oven. In most of the heating experiments, each thermocouple was inserted in a sample of oil to a depth of about one inch above the bottom of the container. In a few of the experiments, one or all of the thermocouples were secured at particular locations in the oven as a check on the temperature of the oven. At the beginning of each heating experiment, the oven was at room temperature as were the oil samples. During the experiments, after the early part of the study, the relative location of the samples in the oven was recorded.

The heating time was noted and recorded from the moment that the heating coils were turned on. The rise in temperature of the oven, as noted on the thermometer at the upper outlet of the chamber, was recorded in most instances at intervals of 5 minutes. When the temperature of the oven, as indicated by the thermometer, had reached 140° C. (or 160° C.), it was maintained for the remainder of the experiment. The temperature of each oil sample was determined, in most instances, every 15 minutes during the first hour and then

every 30 minutes during the remainder of the experiment. This was obtained by recording the temperature of the thermometer at the chamber outlet and the difference in voltage between the reference thermocouple (attached to the thermometer) and the working thermocouple in each oil sample. This voltage difference was later converted to temperature difference from the standardization graph.

The data from the heating trials were plotted on inverted semilog paper according to the method developed by Ball (9) for the thermal process time for canned food. The temperature in degrees Centigrade was plotted logarithmically and the time in minutes linearly. The top temperature line was designated as the maximum chamber temperature minus one, on the assumption made by Ball that the material being heated never fully reached the temperature in the chamber.

For the heating experiments which were conducted using free-flowing steam as the source of heat, steam was allowed to flow at a slow but steady rate into the autoclave chamber, making sure that no elevation of pressure occurred. The door of the autoclave was closed except for the clearance required to permit entrance of the thermocouples. The thermometer and reference thermocouple were secured so that they were exposed to the free-flowing steam in the chamber. As soon as steam was flowing freely, it was found that the temperature within the chamber had reached 100° C. The starting temperature of the oil samples was room temperature. The temperature of the samples was recorded as rapidly as the reading could be made, usually ½ minute from one sample to the next. Otherwise, the procedure was the same as that used in the hot air experiments.

Findings

In all, 62 heating experiments were conducted using hot air and 8 using free-flowing steam. During the hot air procedures, 312 samples of 5 different oils were heated. When using steam as a heat source, 46 samples of oils were heated.

With the oven empty and operating at a maximum temperature of 140° C., it was found that the temperature in the oven, as recorded by thermocouples, was higher than that of the thermometer in the outlet. The temperature gradient within the empty oven ranged from 20 degrees above the temperature of the thermometer at one location on the grill flooring to about 3 degrees above in the upper areas of the

chamber. When the air was circulated by means of the fan, this temperature gradient was slightly reduced.

Rate of Heating of Different Oils

A few heating experiments were conducted to try to determine whether or not different vegetable oils heated at a different rate. Corn oil, cottonseed oil, olive oil, peanut oil, and sesame oil were used. The differences obtained in the heating rates of the different oils were well within those which could be accounted for by the temperature gradient within the oven or by other variable factors to be presented later in this report. Therefore, it would appear that among the oils under test, there was no significant difference in the rate of heating due to the type of oil that was detectable with the method employed. Consequently, since corn oil was readily available in larger quantities, it was selected for use in most of the heating experiments.

It is of interest to note that corn oil was observed to become slightly darker in color upon prolonged heating at 160° C. However, this phenomenon was not investigated since it was a distinct problem by itself and not a part of this study. It was realized that this might not occur with other vegetable oils.

Sterilization by means of dry heat is usually accomplished by heating at 160° C. for not less than 1 to 2 hours. Where this is not possible, due to physical or chemical changes in the oil, a temperature of 140° C. for not less than 4 hours may be employed. In this study, most of the hot air heating experiments were conducted with the thermometer in the outlet of the oven chamber showing a maximum temperature of 140° C. For comparative purposes, a few procedures were conducted using a maximum temperature of 160° C.

Rate of Heating with Natural Convection of Hot Air in Oven

When the oven and its contents were heated by means of natural convection currents within the oven chamber, the heating curve of the oven itself assumed the shape of a parabola. This can be seen in Figures 1 and 2. Figure 1 also shows the heating rate curves of different volumes of corn oil, all contained in Pyrex liter bottles and heated simultaneously. These are from one heating experiment and are representative of those obtained from many procedures. The smaller volumes of corn oil exhibited a rate of heating which provided curves of the same general shape as that of the oven. However, the rate of heating of the larger volumes of oil became less as their

temperatures increased. The curves, therefore, tended to bend slightly toward the abscissa. From Figure 1, it may also be observed that the relation one to another of the rate of heating curves were in the order of the volume of oil but not directly proportional to the volume.

In order to study the effect of container walls of a different material as well as the effect of different surface areas per unit volume of oil and different ratios of height of oil to the diameter, cans commonly available for food and chemical products were employed as containers for oil samples. The heating curves shown in Figure 2 are representative of those obtained from heating different quantities of

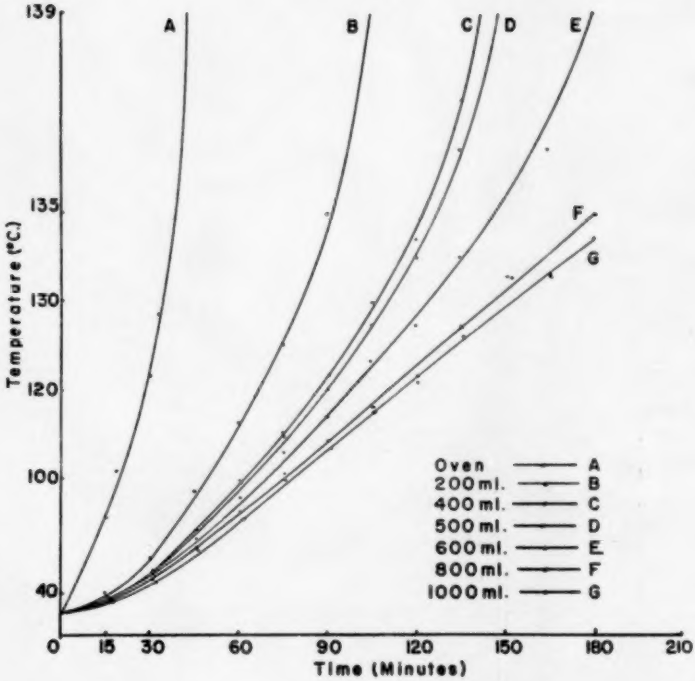

FIGURE 1.

Rate of Heating Corn Oil in Pyrex Liter Bottles with Natural Oven Convection

corn oil in cans at the same time. It will be noted that the shapes of the curves were more irregular than when the oil samples were contained in Pyrex bottles, as shown in Figure 1. The relative order of the heating curves was not the same as the relative order of the volumes. Neither were they in the same relative order as the surface areas, as indicated by the data shown in Table I. It appeared, however, that a can with a larger diameter in relation to its height heated up faster than one with a relatively smaller diameter. This effect may be noted from the data for the can containing 700 ml. and that for

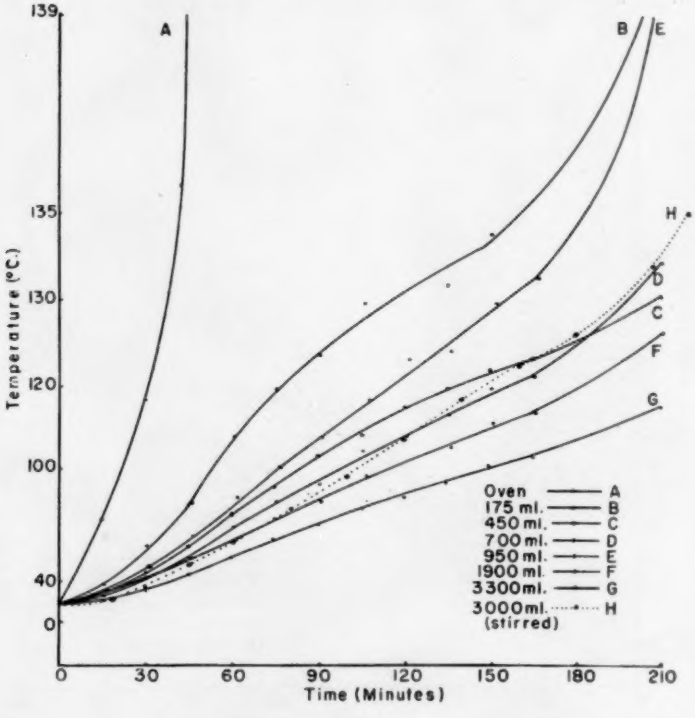

FIGURE 2.

Rate of Heating Corn Oil in Cans of Different Sizes with Natural Oven Convection

the can containing 450 ml. in Table I. In this instance, the larger volume of oil heated faster than the smaller volume, but the diameter of the oil layer of the 700 ml. volume was greater than that of the 450 ml. volume, while the heights were about equal.

TABLE I

Rate of Heating Corn Oil in Cans[a] of Different Sizes With Natural Oven Convection

(See Figure 2)

Volume	Surface Area[b] of Oil	Height	Diameter	Temperature of Oil after 210 Minutes*
175 ml.	180 sq. cm.	8.3 cm.	5.2 cm.	139.5° C.
450 ml.	320 sq. cm.	9.7 cm.	7.5 cm.	130 ° C.
700 ml.	470 sq. cm.	10 cm.	10 cm.	132.5° C.
950 ml.	520 sq. cm.	10.5 cm.	10.5 cm.	139.5° C.
1900 ml.	820 sq. cm.	10 cm.	15 cm.	126.5° C.
3300 ml.	1200 sq. cm.	19 cm.	14.5 cm.	115.5° C.

[a] All heated concurrently.
[b] Total surface area of oil exposed to heat.
* Starting at room temperature (Approx. 20° C.).

By comparing similar volumes of corn oil and noting the rate of heating curves shown in Figures 1 and 2, it will be seen that a similar volume of oil heated more rapidly in a Pyrex bottle than in a can. The one exception to this was the can containing 950 ml. of oil which was entirely out of position as compared with the curves for other volumes of oil in cans. In fact, the corn oil in the can containing 950 ml. reached a temperature of 139.5° C. at exactly the same time as the corn oil in the can containing 175 ml.

A striking difference was obtained when the corn oil in the largest can (3000 ml.) was stirred during the heating procedure by means of the flat metal ring previously described. The dotted line in Figure 2 shows the rate at which the oil then was heated. The rate of heating was significantly more rapid than when a similar volume (3300 ml.) of oil in the same container was not stirred.

Rate of Heating of the Same Container of Corn Oil with Different Oven Loads

The rate of heating of 1000 ml. of corn oil in a Pyrex liter bottle varied with the load, that is, the total volume of oil in the oven. From Table II it can be seen that the time required for the 1000 ml. of corn oil to be heated from room temperature to a temperature of 140° C. varied somewhat irregularly when compared with the total volume of oil in the oven, contained in Pyrex bottles and/or cans, during a particular heating experiment. That is, an increase in the oven load did not necessarily increase the heating time of the 1000 ml. bottle of oil. Actually, there appeared to be a trend to require less time for the 1000 ml. bottle of corn oil to reach a temperature of 140° C. when the oven contained larger loads.

The location of the container in the oven had an influence on the time required to heat the oil in the container to the maximum temperature. However, in the first three experiments listed in Table II, the 1000 ml. Pyrex bottle of oil was located in the same position in the oven. Since these heating times showed the greatest variation, one from another, the location of the container in the oven cannot, apparently, account for the greatest variance in heating times. It should be noted in Table II that in the experiment requiring the least time for the oil to reach a temperature of 140° C., there were present the least number of containers in any of the sets. Furthermore, less time

TABLE II

Effect of Oven Load When Heating 1000 ml. of Corn Oil in Pyrex Liter Bottles With Natural Oven Convection

Total Volume of Oil in Containers (Oven Load)	Number of Containers in Set[a]	Heating Time to 140° C.* of Oven	Heating Time to 140° C.* of 1000 ml. Corn Oil
3,500 ml.	6	45 min.	270 min.
3,500 ml.	6	50 min.	260 min.
4,300 ml.	2	36½ min.	190 min.
6,700 ml.	4	53 min.	210 min.
10,000 ml.	5	62½ min.	240 min.
12,300 ml.	8	75 min.	210 min.

[a] Each set of containers heated separately.
* Starting at room temperature (Approx. 22° C.).

was required for the oven to reach the maximum temperature, even though the load in the oven was slightly greater than during two other experiments.

When the hot air in the oven was circulated by means of the fan during the heating procedure, as previously described, the same 1000 ml. of corn oil in the Pyrex liter bottle as used above, required much less time to reach the temperature of 140° C., as indicated in Table III. From the data given in Table III, it appeared that the total volume of oil in the oven had little effect on the time required for the 1000 ml. of corn oil to reach a temperature of 140° C., when the air was circulated in the oven by means of a fan. The second experiment listed, which showed a much greater heating time as compared with the others, differed in that the cans heated at the same time as the Pyrex bottle had been given an exterior coating of flat black lacquer. This may have provided a factor in bringing about the heating time variation.

TABLE III

Effect of Oven Load When Heating 1000 ml. of Corn Oil in Pyrex Liter Bottles With Forced Circulation of Hot Air in Oven

Total Volume of Oil in Containers (Oven Load)	Number of Containers in Set[a]	Heating Time to 140° C.* of Oven	of 1000 ml. Corn Oil
8,100 ml.	5	70 min.	90 min.
8,700 ml.	6	66 min.	170 min.
9,100 ml.	5	61 min.	110 min.
13,100 ml.	7	78 min.	110 min.
18,000 ml.	10	115 min.	110 min.

[a] Each set of containers heated separately.
* Starting at room temperature (Approx. 28° C.).

Rate of Heating with Forced Circulation of Hot Air in Oven

When the heating curves in Figure 3 are compared with those in Figures 1 or 2, the smoothness of the curves and the consistent parabolic shape of those in Figure 3 are striking. The forced circulation of the hot air in the oven brought about this change in the

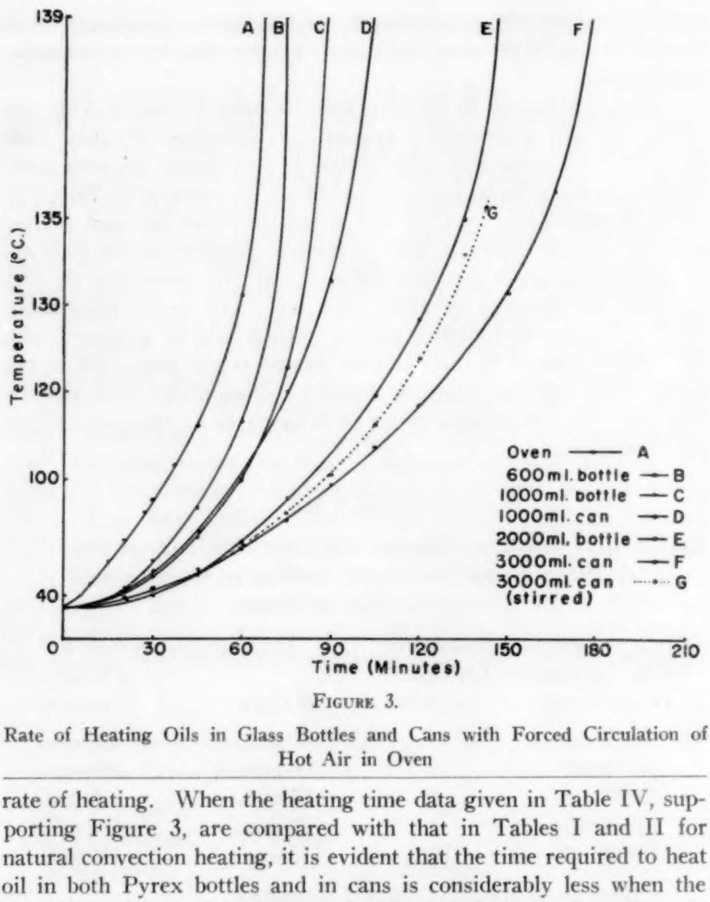

FIGURE 3.

Rate of Heating Oils in Glass Bottles and Cans with Forced Circulation of Hot Air in Oven

rate of heating. When the heating time data given in Table IV, supporting Figure 3, are compared with that in Tables I and II for natural convection heating, it is evident that the time required to heat oil in both Pyrex bottles and in cans is considerably less when the hot air is circulated by means of a fan. When the data given in Table IV are studied further, it may be noted that the heating time for the oil samples is in the same order as compared with the volume, or with the surface area of the oil, whether contained in Pyrex bottles or in cans. However, the heating times are not directly proportional to either the surface area or the volume. It should also be noted that the 1000 ml. of corn oil in a can required longer to reach a temperature of 140° C. than the 1000 ml. of oil in the Pyrex bottle.

TABLE IV

RATE OF HEATING OF OILS IN GLASS BOTTLES AND CANS WITH FORCED CIRCULATION OF HOT AIR IN OVEN [a]

(See Figure 3)

Oil	Volume	Type of Container [b]	Surface Area [c]	Height	Diameter	Time for Oil to Reach 140° C.*
Sesame	600 ml.	Pyrex Liter Bottle	410 sq. cm.	8 cm.	10 cm.	80 min.
Corn	1000 ml.	Pyrex Liter Bottle	550 sq. cm.	12.5 cm.	10 cm.	90 min.
Corn	2000 ml.	Pyrex 2-L. Bottle	915 sq. cm.	17 cm.	12.5 cm.	150 min.
Corn	1000 ml.	Can	555 sq. cm.	11.5 cm.	10.5 cm.	105 min.
Corn	3000 ml.	Can	1080 sq. cm.	20 cm.	13 cm.	180 min.

[a] Time for oven to reach 140° C.—68 minutes.
[b] All containers heated concurrently.
[c] Total surface area of oil exposed to heat.
* Starting at room temperature (Approx. 30° C.).

The data presented in Table V (next to last column) are representative of the rate of heating of oil samples in Pyrex bottles and in cans, the latter having been given an exterior coating of flat black lacquer. From this and similar experiments, it was found that the cans with a flat black coating heated faster than did the Pyrex bottles of similar capacity. Previous to painting the exterior of the same cans black, the Pyrex bottles of similar capacity were found to heat faster than the cans.

TABLE V

RATE OF HEATING OF CORN OIL IN GLASS BOTTLES AND CANS [a] (EXTERIOR PAINTED WITH FLAT BLACK LACQUER) WITH FORCED CIRCULATION OF HOT AIR IN OVEN

Volume	Type of Container	Surface Area [b]	Height	Diameter	Time for Oil to Reach 140° C. [c]	Time for Oil to Reach 160° C. [d]
200 ml.	Black Can	185 sq. cm.	4 cm.	7.5 cm.	100 min.	100 min.
500 ml.	Black Can	380 sq. cm.	7 cm.	10 cm.	110 min.	130 min.
2000 ml.	Black Can	830 sq. cm.	10 cm.	15 cm.	120 min.	160 min.
3000 ml.	Black Can	1080 sq. cm.	20 cm.	13 cm.	180 min.	220 min.
1000 ml.	Pyrex Liter Bottle	550 sq. cm.	12.5 cm.	10 cm.	175 min.	165 min.
2000 ml.	Pyrex 2-L. Bottle	915 sq. cm.	17 cm.	12.5 cm.	145 min.	220 min.

[a] All containers in each experiment heated concurrently.
[b] Total surface area of oil exposed to heat.
[c] Starting at room temperature (Approx. 22° C.). Time for oven to reach 140° C. —66 minutes.
[d] Starting at room temperature (Approx. 24° C.). Time for oven to reach 160° C. —88 minutes.

Rate of Heating with Asbestos Plate Under Containers

In order to try to obtain some indication of the effect of heat transfer directly from the heating coils to the samples, an asbestos plate was placed upon the grill floor of the oven and the containers of oil were placed upon the asbestos plate. A space of about 1½ inches remained between the edge of the asbestos plate and the sides of the oven to allow circulation of the hot air by the fan. From the data given in Table VI, when compared with that given in Table IV, it may be noted that the heating time was longer when the asbestos plate was used. The differences in the heating times of equal volumes of oil heated at the same time in containers of the same type and capacity were quite marked, as can be noted from Table VI. The reason for this variation is not clear. However, the circulation in the oven was definitely affected by the presence of the asbestos plate.

TABLE VI

Rate of Heating of Oils in Glass Containers With Asbestos Plate Under Containers [a] and With Forced Circulation of Hot Air in Oven [b]

Oil	Volume	Surface Area [c]	Height	Diameter	Time for Oil to Reach 140° C.*
Corn	100 ml.	125 sq. cm.	5.5 cm.	5 cm.	100 min.
Corn	1000 ml.	550 sq. cm.	12.5 cm.	10 cm.	185 min.
Olive	1000 ml.	550 sq. cm.	12.5 cm.	10 cm.	160 min.
Corn	2000 ml.	915 sq. cm.	17 cm.	12.5 cm.	185 min.
Corn	2000 ml.	915 sq. cm.	17 cm.	12.5 cm.	175 min.
Corn	2000 ml.	915 sq. cm.	17 cm.	12.5 cm.	225 min.

[a] All containers heated concurrently. Containers were: 100 ml. vial, 1-liter and 2-liter Pyrex bottles.

[b] Time for oven to reach 140° C.—72 minutes.

[c] Total surface area of oil exposed to heat.

* Starting at room temperature (Approx. 22° C,).

Rate of Heating to a Maximum Oven Temperature of 160° C.

A few experiments were conducted to study the effect of attaining and maintaining a maximum oven temperature of 160° C. instead

of the 140° C. used in most of the heating experiments. The last column of Table V gives the data obtained from such an experiment, the latter being a duplicate of the one from which the data in next to the last column of the same table were obtained, except that the maximum oven temperature was higher. The general trend was in the direction of a slight increase in the heating time for the oil to reach the higher oven temperature (160° C.), as would be expected.

Replicate Rate of Heating to a Maximum Oven Temperature of 140° C.

Eight replicate heating experiments were conducted using the fan to circulate the hot air in the oven with the maximum temperature at the outlet of the oven chamber at 140° C. The same containers of oil were used in each experiment and they were located in exactly the same location in the oven. The same thermocouples were placed in the same containers of oil at the same depth in the oil. One variance noted was that, during Experiment 2, the speed of the fan was irregular.

Table VII shows the heating time in minutes required for the six containers of oil listed to reach the temperature of the oven during the 8 replicate experiments. The differences found were rather startling, particularly among the replicate heatings with a black can containing 2000 ml. and among those with a Pyrex bottle containing 2000 ml. of corn oil. A black can containing 3000 ml. of oil showed the least variation from one experiment to another. It should be noted that experiments 5, 7, and 8 showed little variance in the heating time of the same containers of oil and also of the oven. Though the heating times of the oil samples in experiments 3 and 6 also correlated well with those in 5, 7, and 8, the oven heating times did not correlate well. Here, as elsewhere in this report, findings were reported as observed.

Rate of Heating by Steam as Compared to Hot Air

A few heating experiments were conducted using free-flowing steam as the source of heat instead of hot air. The data presented

TABLE VII

RATE OF HEATING OF CORN OIL IN GLASS BOTTLES AND CANS WITH FORCED CIRCULATION OF HOT AIR IN OVEN—HEATING TIME IN MINUTES REQUIRED WITH REPLICATE EXPERIMENTS TO OVEN MAXIMUM OF 140° C.

Volume	Type of Container [a]	Experiment [b] 1	Experiment 2	Experiment 3	Experiment 4	Experiment 5	Experiment 6	Experiment 7	Experiment 8
200 ml.	Black Can	100	90	115	95	110	120	110	100
500 ml.	Black Can	110	120	145	120	160	160	145	150
2000 ml.	Black Can	120	165	245	150	240	240	230	240
3000 ml.	Black Can	180	195	195	185	190	190	175	175
1000 ml.	Pyrex Bottle	180	200	150	130	165	170	140	150
2000 ml.	Pyrex Bottle	145	190	265	160	280	260	260	260
Oven Heating Time:		66	50	82	61	56	76	58	57
Starting Temperature:		22° C.	26° C.	24° C.	22° C.	23° C.	21° C.	20° C.	20° C.

[a] For dimensions of containers, see Table V.

[b] All containers in each experiment heated concurrently.

in Table VIII show a comparison between a representative steam heat experiment and a hot air heat experiment, the latter having the air circulated by means of the fan. For comparative purposes, the tabulated heating times for oil samples when heated by steam and when heated by hot air are the times required for the temperature of the sample to rise from room temperature to a temperature of 100° C. As would be expected, the oil samples were heated by the steam more rapidly than by the hot air. The steam heated the containers of oil over the same temperature increment in approximately one-half the time. The oil samples in unpainted cans were heated by the steam slightly more rapidly than the oil in the Pyrex bottles.

TABLE VIII

RATE OF HEATING OF OILS IN GLASS BOTTLES AND CANS[a] WITH FORCED CIRCULATION OF HOT AIR IN OVEN AND WITH FREE-FLOWING STEAM

Source of Heat	Oil	Volume	Type of Container	Time for Oil To Reach 100° C.*
Hot Air	Corn	200 ml.	Black Can	50 min.
Hot Air	Corn	500 ml.	Black Can	60 min.
Hot Air	Corn	2000 ml.	Black Can	65 min.
Hot Air	Corn	3000 ml.	Black Can	90 min.
Hot Air	Corn	1000 ml.	Pyrex Liter Bottle	80 min.
Hot Air	Corn	2000 ml.	Pyrex 2-L. Bottle	75 min.
Steam	Cottonseed	500 ml.	Shiny Can	38 min.
Steam	Olive	800 ml.	Pyrex Liter Bottle	42 min.
Steam	Corn	1000 ml.	Shiny Can	42 min.
Steam	Corn	2000 ml.	Pyrex 2-L. Bottle	50 min.
Steam	Corn	3300 ml.	Shiny Can	50 min.

[a] The first 6 containers were heated concurrently; the last 5 containers were heated concurrently.

* Starting at room temperature (Approx. 22° C.).

Summary and Conclusions

A series of 70 heating experiments, employing either dry or moist heat, were conducted to determine the time required for volumes ranging from 10 to 3600 ml. of 5 different vegetable oils, mostly corn oil, to heat from room temperature to one of three temperatures, namely, 100° C., 140° C., or 160° C. Of the experiments, 59 were performed in an electric natural convection type hot air oven with 140° C. as the maximum oven temperature attained. Three were conducted with 160° C. as the maximum oven temperature attained. Of the 62 hot air heating experiments, 38 were performed by natural convection heating and 24 were performed by circulating the hot air in the oven by means of a fan. Eight experiments were carried out using an autoclave with free-flowing steam at 100° C. as the source of heat.

When the thermometer in the outlet of the oven recorded the temperature of 140° C., or 160° C., the thermostat control was set to maintain that temperature during the remainder of the experiment. When steam was flowing freely from the outlet of the autoclave, a temperature of 100° C. had been attained and was so recorded. Both the equipment and the oil samples were at room temperature at the beginning of each experiment.

During most of the procedures, six samples of oil contained in various Pyrex glass containers or cans were heated at one time. The dimensions for the oil layer in each of the containers were recorded as well as the volume. The position of the containers in the oven was also recorded.

The introduction of the fan to increase the circulation of the hot air within the oven markedly increased the efficiency of heating of the corn oil in all containers. The corn oil in one can was stirred during heating. This stirring increased the efficiency of heating. With stirring, a more rapid heating of the oil was particularly evident during natural convection heating, but also, to a smaller degree, during heating with forced circulation of the air in the oven. During a few experiments, an asbestos plate was placed under the samples of oil to ascertain the effect of direct heat transfer from the heating elements of the oven. As anticipated, the oil samples heated at a much slower rate when the asbestos plate was used. However, no improvement in the interrelationships of the heating time of oil samples was observed.

The effect of the total volume of oil in the oven during a series of heating experiments was investigated, in relation to the rate of heating of a particular container of oil. A larger load in the oven appeared to provide a more efficient heating situation in some cases, since a Pyrex bottle containing 1000 ml. of corn oil heated to oven temperature in less time with a relatively large oven load than with a smaller load.

When the outer surfaces of cans were painted with flat black lacquer, it was found that corn oil in these black cans heated more rapidly than a similar volume in cans not painted.

From the data obtained, it can be concluded that numerous factors influenced the rate of heating. The variable factors were such that repeated heatings, planned as duplicate trials of previous hot air heating experiments, did not necessarily provide the same temperature increase of the same oil sample during a given period of time. As a result of these variable factors, it was not found possible to predict the time required to heat containers of oil. This was true whether the heating time of the oil sample was related to the heating time of the oven or to the controlled container variables of volume, surface area, or the dimensional proportions.

Steam heated a particular oil sample from room temperature to a designated temperature (100° C.) in about one-half the time required by hot air heating.

The data obtained have been presented as observed. The variability of the results has made it possible to draw only limited conclusions. It would appear from this study that the measurement of the temperature of the oil in each and every hot air heating situation would be the only sure way of knowing when the oil had reached the designated temperature for sterilization.

Acknowledgment

Grateful acknowledgment is given for the invaluable guidance and counsel of Dr. Grafton Chase.

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SELECTED ABSTRACTS

A Clinical Trial of BZ 55 in the Treatment of Diabetes. Duncan, L. J. P., Baird, J. D., and Dunlop, D. M. *Brit. Med. J.* No. 4990:433 (1956). The sulfonamide compound, BZ 55(N-butyl-N'-sulfanilylurea), was used for the oral treatment of mild diabetes in a group of patients over 45 years of age who were not more than 10 per cent over-weight and who, on a restricted diet, continued to show hyperglycemia and glycosuria and diabetic symptoms in the absence of insulin therapy. Initially, 65 patients were selected but 21 were withdrawn from the study because of severe ketosis upon the withdrawal of insulin, very high blood glucose concentrations, or because adequate control of the diabetic symptoms was obtained with dietary control alone. Of the remaining 44 patients, 33 responded well to treatment with BZ 55.

The dosage employed was 3 to 4.5 Gm. before breakfast each day. If response was satisfactory, the dose was gradually reduced after one or a few days to a maintenance dose of 1 to 1.5 Gm. daily. Among the patients showing satisfactory clinical control from this drug, the reduction in glycemia ranged from 65 to 160 mg. per 100 ml. Among the patients who were not satisfactorily controlled, some showed a reduction in glycemia of 60 to 90 mg. per 100 ml. However, this was not enough to establish clinical control because of the very high initial glucose levels in the blood.

The authors pointed out that the clinical control of certain diabetics by BZ 55 was apparently brought about by a reduction in the fasting glucose blood level. Glucose tolerance was not changed, however, and there was no alteration in the daily profile of glycemia although glycosuria was reduced or eliminated. BZ 55 appeared to be completely contraindicated in patients with a marked tendency to develop ketosis. Use of the drug should not supplant dietetic restriction. There was great danger in the withdrawal of insulin in those patients who did not respond to BZ 55 therapy. It was found in follow-up studies that maintenance therapy must be continuous. A high incidence of toxic effects were observed, such as, skin reactions, drug fever, slight granulocytopenia, and thrombocytopenia.

The Treatment of the Common Cold with Bioflavonoids and Ascorbic Acid. Tebrock, H. E., Arminio, J. J., and Johnston, J. H. *J. A. M. A. 162:*1227 (1956). A controlled, double-blind evaluative trial of the effectiveness of the bioflavonoids and/or ascorbic acid on the common cold was conducted on over 1900 persons. The patients were divided into four approximately equal treatment groups. Each group received one of the following four times a day: 250 mg. of bioflavonoids plus 50 mg. of ascorbic acid, 250 mg. of bioflavonoids, 50 mg. of ascorbic acid, or a placebo. In addition, every patient received a preparation commonly used for subjective control of the common cold containing, 325 mg. of salicylamide, 195 mg. of acetophenetidin, 65 mg. of caffeine, and 50 mg. of thonzylamine hydrochloride.

Tables were presented to show the mean number of colds, the sex, and the age of the treatment groups as an indication of the random distribution of the susceptibility to colds of the patients in the groups. Tables were also given to show the results obtained from therapy based upon subjective and objective changes, decrease in tabulated symptoms, change in nasal secretions, decrease in nasal obstruction, decrease in pharyngitis, and the differences in mean number of work days lost. From the results obtained, the authors concluded that the bioflavonoids, ascorbic acid, or a combination of these agents, in the dosage employed, had no significant effect upon the course of the common cold. While the authors recognized that the argument might be advanced that larger doses of these agents might produce greater effects, they pointed out that the dosages which were given were those normally considered to be adequate to affect the capillary permeability. They felt that, since these doses were not significantly more effective in the treatment of the common cold than usual symptomatic therapy, there was no reason to believe that larger doses would be effective either.

A Clinical Evaluation of the Hypoglycemic Agent BZ 55. Hunt, J. A., Oakley, W., and Lawrence, R. D. *Brit. Med. J.* No. 4990:445 (1956). Two groups of patients were treated with the new hypoglycemic agent, BZ 55(N-butyl-N′-sulfanilylurea). The first group of 21 patients was unselected and the patients were representative in respect to age, weight, duration and severity of diabetes, and in insulin requirement. The maximum daily dose ranged from 1 to

4 Gm. Several broad conclusions were drawn by the authors following the treatment of this group of patients. Young diabetics and those requiring relatively large doses of insulin showed little response to therapy with BZ 55. These patients also showed no reduction in insulin requirement while receiving BZ 55. No constant relationship could be demonstrated between the response to therapy and the age of the patient, the duration of the diabetes, or the duration of insulin therapy. Responsiveness to BZ 55 therapy seemed to be associated with the factors of age of onset of the diabetes, over 40 years in all cases; and absence of more than slight ketonuria while on dietary control without insulin.

Based upon the findings from therapy in the first group of patients, a second group of 17 patients was selected. All of these patients had developed diabetes after they were 40 years of age, none of them showed appreciable ketonuria without insulin, none were grossly overweight, and diet alone failed to control the diabetes. In this group, there was a good to moderate response to therapy with BZ 55 in every case. The daily dose ranged from 0.5 to 2 Gm. Side effects such as giddiness developed in 3 patients, an erythematous rash in 3 patients, and drug fever in 1 patient.

The authors concluded that the basis for selection of patients, as used for the second group, seemed to be reasonably correct in predicting which patients would most likely benefit most from therapy with BZ 55.

A Combined Treatment for Amebiasis. Loughlin, E. H., and Mullin, W. G. *Antibiot. Med. & Clin. Ther. 3:*120 (1956). Thirty cases of chronic intestinal amebiasis were treated with a combination of 350 mg. diiodohydroxyquinoline, 50 mg. chloroquine diphosphate, 1000 units bacitracin, and 4000 units neomycin as the sulfate. These ingredients were contained in a single tablet. The dosage regimen was: 1 tablet twice a day for children less than 5 years of age, 1 tablet 3 times a day for children 5 to 10 years of age, and 2 tablets 3 times a day to children over 10 years of age and adults. The tablets were given after meals for a period of 10 consecutive days.

In 22 of these cases, the disease could be credibly ascribed to infection with *Endamoeba histolytica* while in the other 8, though it was surmised that the symptoms were due to amebic infection, the causative agent was difficult to evaluate because of the presence of multiple parasitisms.

In all of the 30 cases reported, the feces were negative to cystic examinations immediately after the course of treatment or shortly thereafter. Thirteen of these patients were observed for 4 to 6 months after treatment. None of them showed a recurrence of cysts in the feces. There was also a striking absence of toxic side effects from the administration of this combination. The authors suggested that the reduced dosage of some of the components in the combination as compared to their dosage when given alone probably accounted for the absence of toxic side effects. They also emphasized the superiority of the results obtained in these 30 cases treated with the combination as compared with treatment with the ingredients singly or in sequence.

Infantile Gastro-Enteritis Treated with Phthalylsulfacetamide and Neomycin. Rogers, K. B., Benson, R. P., Foster, W. P., Jones, L. F., Butler, E. B., and Williams, T. C. *The Lancet* No. 6943:599 (1956). An epidemic of infantile gastro-enteritis in a hospital is, preferably, treated with a chemotherapeutic agent which has been given a controlled clinical trial previously and has been tested *in vitro* against the particular causative strains of bacteria as isolated from the patients. This procedure is not always possible in an emergency.

The authors reported on a controlled trial with phthalylsulfacetamide. Fourteen adult healthy volunteers took as much as 16 Gm. daily. There was no predictable reduction in the bacterial content of the feces, although in a few cases there was a reduction in the number of bacteria. In every volunteer there was a distressing disturbance of bowel function marked by increased and watery stools, borborygmi, colic and tenesmus. Therefore, this drug was not used clinically for the treatment of infantile gastro-enteritis.

When neomycin became available, it was used clinically without a controlled trial. The strains of *Escherichia coli* causing an epidemic of gastro-enteritis among infants in the hospital were found to be sensitive *in vitro* to neomycin although insensitive to chloramphenicol, aureomycin, oxytetracycline, sulfadiazine, sulfadimidine, and sulfamerazine. The dosage employed was 20 mg. of neomycin sulfate per lb. of body weight each day. In all, 101 infants infected with various strains of *E. coli* were treated. All of the infants who were ill responded well to neomycin therapy. Improvement occurred in an average of 2 days after the beginning of therapy and the feces became free from the specific causative agent. Those infants who were car-

riers did not develop enteritis if treatment with neomycin was started early. Only one infant had a clinical relapse but 18 per cent had bacteriological relapses. In the latter cases, the pathogenic strain of *E. coli* reappeared in the feces an average of 6 days after treatment was stopped. Several strains of staphylococci isolated from cases of enteritis were also tested for sensitivity to neomycin. None were found to be insensitive.

The Oral Use of Penicillamine in the Treatment of Wilson's Disease. Walshe, J. M. *Am. J. Med. 21:*487 (1956). Wilson's disease is characterized by an increased concentration of copper in both the liver and brain, an increased excretion of copper in the urine, a low plasma concentration of copper, and a very low level of ceruloplasmin, the copper-binding alpha globulin. The administration of BAL over a prolonged period of time has been shown to produce marked clinical improvement by increasing the excretion of copper. However, severe toxic reactions to BAL develop in some patients.

The author reported on a preliminary study of the effect of penicillamine (dimethyl cysteine), a degradation product of penicillin, in increasing copper excretion. Three doses of 300 mg. of penicillamine were given orally before meals to two normal subjects. Each of these subjects showed a twenty-fold increase in the 24-hour urinary excretion of copper, from about 30 gamma to over 600 gamma. In six patients with Wilson's disease, a similar increase in excreted copper was obtained following the oral administration of from 0.5 to 1.5 Gm. of penicillamine. When BAL was administered to the same patients, the excreted copper was less than that from penicillamine in all but one patient.

A number of other organic compounds containing active sulfur were also administered, but none of them showed activity in promoting copper excretion in the patients with Wilson's disease. These compounds included methionine, tetramethyl cysteine, cysteine, cystamine, penicillin, thiourea, diethyl dithiol terephthalic acid, and d,l-alanine.

The author stated that no toxic reactions were observed in any of the patients given penicillamine during this short term trial. He also indicated that, theoretically, penicillamine should have potential value in the treatment of heavy metal poisoning with compounds of gold and mercury.

BOOK NOTICES AND REVIEWS

The Merck Manual of Diagnosis and Therapy, Ninth Edition. 1888 pp. including index. 1956,Merck & Co., Rahway, N. J. Price $6.75, Deluxe Edition $9.00.

The popularity of this well-known pocket-sized reference can be seen by the sales of the eighth edition published in 1950. Since that time more than 360,000 copies were sold in both English and the Spanish translation.

Over one hundred leading clinicians in the United States served as authors and consultants in preparing the ninth edition.

The arrangement of the text follows the same general pattern as that in previous editions with Part I divided into disease categories following the customary classification. Each disease category is further subdivided into specific disease states and then their symptoms and signs, diagnosis and treatment considered. Of particular interest to pharmacists are the typical prescriptions totalling more than 1600. Those which are pertinent are given at the end of each disease category.

Part II presents chapters on Immunization Procedures, Clinical Procedures, Bedside Procedures, Diets and others.

The number of illustrations has been increased and more tables are found than in previous editions.

The Merck Manual has achieved a place of distinction since it was first published in 1889.

While it obviously could not in a pocket-sized single volume present the whole practice of medicine, it achieves much in this direction. To the young resident or interne it is almost irreplaceable and even to the experienced physician it is of value. To those associated with practitioners of medicine, such as pharmacists, it is extremely useful in gaining a better understanding of disease states and their treatment so that the therapy and the medicinals employed can be seen in broader perspective.

L. F. Tice

The Extra Pharmacopoeia (Martindale) Twenty-Third Edition, Vol. II. Published by direction of the Council of the Pharmaceutical Society of Great Britain xxxi + 1501 pp. including index. 1955, The Pharmaceutical Press, 17 Bloomsbury Square W. C. 1, London. Price £2. 17s. 6d.

Since the fifteenth edition of the Extra Pharmacopoeia in 1912 it has been customary, and indeed necessary, to publish it in two volumes. Volume I contains most of the general information on drugs and medicinals while Volume II is largely devoted to more specialized chapters on various techniques and procedures.

Volume II of the twenty-third edition has been revised, rearranged and enlarged. The first few hundred pages contain analytical addenda to the drugs in Volume I. Then come special chapters devoted to such subjects as: Hydrogen-Ion Concentration, Oxidation-Reduction Potentials, Polarographic Analysis, Ion-Exchange Resins, Titration in Non-aqueous Media, Chromatographic Analysis, Microbiological Assay of Vitamins, Food Analysis, Sterilization, Radiotherapy, and Hematology—to give but a partial list.

Those who have used the Extra Pharmacopoeia over the years need not be told that it probably ranks as the most valuable reference in British Pharmacy and, despite its small size, it contains as much information as one might find in a whole shelf full of ordinary books. The reader will need good vision for the print is quite small (as it must be). In many respects the Extra Pharmacopoeia, if both volumes are at hand, compares in scope with the United States Dispensatory yet each contains much not found in the other work. A good pharmaceutical library would surely list the Extra Pharmacopoeia as among those references that are indispensable.

L. F. Tice

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

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Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

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